6. The disease, though wide-spread and occurring in localities where typhoid fever is present, is comparatively rare.
7. Every instance of negative Widal reaction is not due to infection with paratyphoid bacilli.

We are greatly indebted to Dr. B. H. Buxton, of the Cornell Medical School, for sending us his own organism and those which he obtained from Germany.

REPORT OF A CASE OF PARATYPHOID FEVER.

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Under the title "Infections Paratyphoïdiques," Achard and Bensaude[1] reported in 1896 two cases of continued fever, closely resembling typhoid fever, from which organisms were isolated, intermediate in character, between the typhoid and colon groups. The first case, a young woman, was admitted to the Beaujon Hospital, in Paris, with what at first appeared to be a mild attack of typhoid fever. Though the temperature remained elevated and typhoid in character for forty-six days, no rose-spots were visible, nor was the spleen greatly enlarged. She had no headache, delirium, abdominal distention, or tenderness, but throughout the febrile period there was profuse, often bloody diarrhœa. On the nineteenth day of the disease the left deltoid muscle became inflamed, and for five days the left arm was paralyzed. At this time a large amount of pus was observed in the urine. This persisted for forty-five days, or well into the period of convalescence. On the twenty-fourth day the right femoral vein became inflamed, and on the fortieth day a similar complication appeared on the left side. Throughout the disease there was no leucocytosis, and the Widal reaction was persistently negative.

From a catheterized specimen of urine they isolated an intermediate bacillus. Cultures from the blood were negative, and only B. coli was isolated from the stools. The patient's serum readily agglutinated the organism obtained from the urine, even several weeks after complete recovery. As the urine continued to show a trace of albumin some time after the disappearance of the pus the case was regarded as one of pyelonephritis.

The second case, also seen in Paris, was a child seven months old, who, in June, 1896, had an attack of bronchitis, accompanied by high fever. The few râles which were at first heard soon disappeared, but the temperature remained elevated, terminating by lysis on the twentieth day. Throughout the illness the child was constipated, with meteorism and slight abdominal pain. A few days after the onset an extensive crop of rose-spots appeared on the abdomen and was quickly followed by a scarlatiniform rash over the back and neck. No eruption was visible upon the pharynx. On the thirteenth day of the disease a red, painful swelling was noticed over the right sternoclavicular articulation. The following day fluctuation was made out and an incision revealed a small amount of pus apparently originating in the joint. The cartilage and bone were normal, and the wound healed rapidly. Cultures from the pus showed an organism in every respect similar to the one isolated from the first case. No agglutination tests were made with the child's serum.

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[1] Bull. et Mém. de la Soc. Méd. des Hôpitaux de Paris, 1896, vol. xiii. p. 820.

These bacilli were short rods, with rounded ends, possessing ten to twelve very fragile flagella, and were very actively motile. Their growth in bouillon, in gelatin, and in milk resembled that of B. typhosus. On potato it resembled B. coli. No indol was formed in Dunham's medium. They produced gas in the presence of glucose, but failed to ferment lactose. The sera of immunized animals agglutinated these two organisms, but had no effect upon B. typhosus and B. psittacosis. Their pathogenicity for laboratory animals was much less than that of B. psittacosis.

Achard and Bensaude concluded that their two cases were not similar to those described as due to infection with B. psittacosis, and pointed out the necessity of testing the sera of typhoid fever patients in whom the Widal reaction was absent with these newly discovered organisms. They also advanced the view that when a sufficient number of similar cases should be collected there would be found to exist a type of disease closely resembling typhoid fever, but possessing certain definite and distinguishing characteristics.

Shortly after this Bensaude[1] reported that the organisms first described by him as "paratyphoid" were identical, except in their pathogenicity, with B. psittacosis, and another observer[2] classed these two cases with other instances of psittacosis infection.

The B. psittacosis was isolated by Nocard during an epidemic of "infectious pneumonia," which, in 1892, followed the importation into Paris of several hundred South American parrots. This epidemic made such a deep impression upon the professional minds of that city that for several years many imperfectly reported cases of obscure continued fever, both with and without pulmonary complications, were described as instances of "La Psittacose." The exact nature of many of these cases cannot now be determined. The true disease has, however, been accurately described,[1] and there can be no doubt that, in spite of the similarity between the "paratyphoid" and psittacosis organisms, the clinical picture of the two cases of Achard and Bensaude is similar not to that of "infectious pneumonia," but to that of the rapidly growing group of cases now under consideration.

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[1] Thesis, Paris, 1897.

[2] Millienne. Thesis, Paris, 1897.

In 1897 Widal and Nobécourt[2] described an organism isolated from an abscess in the neighborhood of the thyroid gland which also possessed the cultural characters of the B. psittacosis without giving its serum reactions. This "paracolon bacillus" was agglutinated by the patient's own blood in a dilution of 1 to 1000.

One year later Gwyn[3] reported a case from Dr. Osler's clinic which presented a typical picture of typhoid fever, stupor, delirium, continued temperature, rose-spots, palpable spleen, diazo reaction, and intestinal hemorrhage. From the blood of this patient Gwyn obtained a bacillus which was similar in character to Widal's paracolon bacillus. The patient's serum agglutinated this bacillus in a dilution of 1 to 200, but did not agglutinate the typhoid bacillus in dilutions above 1 to 5. Gwyn seems to have regarded this case as one of typhoid fever, with a secondary paracolon infection, although he raises the question as to whether all the symptoms might not have been due to a paracolon infection alone.

In 1900 Cushing[4] described an organism, Bacillus O, isolated from a costo-chondral abscess following a supposed attack of typhoid fever. The Bacillus "O" was agglutinated by the patient's own blood in a dilution of 1 to 800. Culturally the organism showed only minor variations from Gwyn's paracolon bacillus, but the serum of Cushing's patient did not agglutinate Gwyn's organism. In an elaborate study of the characters of these bacilli, Cushing showed their apparently close relationship to the enteritidis group, intermediate in character between the colon and typhoid groups. He summarized the chief distinguishing features of this group as follows:

"*Intermediate Group.* B. Gärtner and B. chol. suis type. Bacilli with the morphology of B. typhosus and possessing an equal or greater number of flagellæ. Actively motile and in many cases having a distinct pathogenicity for both man and animals. Reaction in milk presents an early and terminal strong alkalinity in the presence of air, appearing after a transient acidity. Milk is never coagulated. They ferment glucose with the production of gas, never lactose or saccharose. Under ordinary cultural conditions no indol is produced.

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[1] Dujardin-Beaumetz. Official Report, Paris, 1892. Gilbert and Fournier. Etude sur la Psittacose. La Presse Médicale, 1897, vol. v. p. 25.

[2] Séroréaction dans une infection à paracolibacille. La Sémaine Médicale, 1897, vol. xvii. p. 285.

[3] On Infection with a Paracolon Bacillus in a Case with All the Clinical Features of Typhoid Fever. Johns Hopkins Hospital Bulletin, 1898, vol. ix. p. 54.

[4] A Comparative Study of Some Members of a Pathogenic Group of Bacilli of the Hog Cholera or Bac. Enteritidis (Gartner) Type, Intermediate Between the Typhoid and Colon Groups. Johns Hopkins Hospital Bulletin, 1900, vol. xi. p. 156.

"Bacillus "O" and B. paracolon (Gwyn) may represent a subdivision of this group, being slower in their action on milk and growing less luxuriantly, and move like B. typhosus in various fluid media and resembling it in their pathogenic action on animals."

Durham[1] later attempted to separate Gwyn's paracolon and Cushing's Bacillus "O" from the members of the enteritidis group, distinguishing them chiefly by their growth in litmus whey and by their inability to form free gas from glucose in a Witte's peptone solution.

In 1900 Schottmüller[2] reported a case similar to Gwyn's, and later, in 1901, he reported five more such.[3] Each patient presented the clinical features of typhoid fever without showing a Widal reaction toward typhoid bacilli. From the blood of each of these cases he isolated bacilli which were identical or closely related and which presented the characteristics of Gwyn's paracolon bacillus. In each case the bacilli were agglutinated by high dilutions of serum from the same patient, while typhoid bacilli were unaffected by dilutions of 1 to 33. According to Schottmüller, the bacilli isolated were not all identical in character, but so closely related as to form a fairly well-defined group. In this group he recognized two types, A and B, depending upon the appearance of the growth upon gelatin and potato, the alkali formation in litmus whey, and the serum reactions. In addition to these six cases, Schottmüller reported a seventh infection which occurred in a doctor who had worked with one of his (Schottmüller's) cultures. Although no organisms were cultivated from the blood of this patient, his serum agglutinated the bacilli obtained from certain of the other cases, and he was believed to be suffering from a similar infection.

Recently, under the name of Bremen gastric fever, Kurth[4] has described five cases with many of the features of enteric fever, but without Widal reactions. From the feces of one of his patients and from the urine of another he isolated bacilli which were agglutinated by high dilutions of the serum of four of the cases. The serum of the fifth, the case showing bacilli in the urine, was unfortunately not preserved, and so could not be tested. Kurth's organisms differed in some respects from Gwyn's, Cushing's, and Schottmüller's. They were very pathogenic to mice and guinea-pigs, producing a septicæmia. A membrane was formed on bouillon, and milk showed a late coagulation. In glucose bouillon gas was produced. No note is made of the action on the other sugars. Indol was not formed after forty-eight hours. Without further study one would be inclined to doubt the affinity of Kurth's bacilli to the group that we have been describing.

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[1] Some Theoretical Considerations upon the Nature of Agglutinins, together with Further Observations upon Bacillus Typhi Abdominalis, Bacillus Enteritidis, Bacillus Coli Communis, Bacillus Lactis Aerogenes, and some other Bacilli of Allied Character. Journal of Experimental Medicine, 1901, vol. v. 353.

[2] Ueber eine das Bild des Typhus bietende Erkrankung hervorgerufen durch Typhus ähnliche Bacillen. Deut. med. Wochenschr., 1900, vol. xxvi. p. 511.

[3] Weitere Mittheilungen über mehrere das Bild des Typhus bietende Krankheitsfälle hervorgerufen durch typhusähnliche Bacillen (Paratyphus). Zeitschr. f. Hygiene u. Infectionskr., 1901, vol. xxxvi p. 368.

[4] Ueber typhusähnliche durch einen bisher nicht beschriebenen Bacillus (Bacillus bremensis febris gastricæ) bedingte Erkrankungen. Deut. med. Wochenschr., 1901, vol. xxvii. pp. 501 and 519.

Brion and Kayser have reported a case[1] in which an organism having the characteristics of the bacilli belonging to type A of Schottmüller was isolated from the blood, urine, feces, vagina, and rose-spots. The patient was a young girl, who entered the hospital in the third week of her illness. The temperature was slightly elevated and somewhat irregular. There was anorexia, abdominal pain, and constipation. The spleen was palpable, but no rose-spots were noted. A profuse vaginal discharge was found, cover-slips from which showed gonococci. In eight days the temperature reached normal, and six days later the patient was discharged. She returned to the hospital after three days with symptoms pointing to a relapse of the original illness. At this time the spleen was palpable and definite rose-spots were seen over the abdomen. Following this relapse there was a second one, which occurred after an interval of normal temperature for several days. During convalescence symptoms of thrombosis developed in the left leg. The Widal reaction was absent throughout the attack, and the organism isolated from so many different situations reacted positively with the patient's serum in 1 to 1000 dilutions.

A case of typhoid fever with secondary infection by a "paracolon" bacillus has been observed by Sibman.[2] The patient presented the symptoms of cholecystitis, and the "paracolon" bacillus was isolated from the gall-bladder, blood, and urinary bladder during life. This organism agglutinated with the patient's serum in dilutions of 1 to 20, but reaction was also obtained in much higher dilutions (1 to 250) with bacillus typhosus. At autopsy healing ulcers were found in the ileum.

Hume's case[3] presented typical typhoidal symptoms, rose-spots, enlarged spleen, and a relapse. The diarrhœa was profuse and persisted for more than a month after the temperature became normal. Intestinal hemorrhages were present. A cystitis occurred during convalescence, and this led to the cultivation from the urine of an intermediate bacillus which was also isolated later from the feces. The patient's serum agglutinated this organism in a dilution of 1 to 200, but did not affect the typhoid bacillus in a dilution of 1 to 10

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[1] Ueber eine Erkrankung mit dem Befund eines typhusähnlichen Bacteriums im Blute (Paratyphus). Münchener med. Wochenschrift, 1902, No. 15, p. 611.

[2] Boston Medical and Surgical Journ., 1902, No. 17, vol. cxlvi. p. 443.

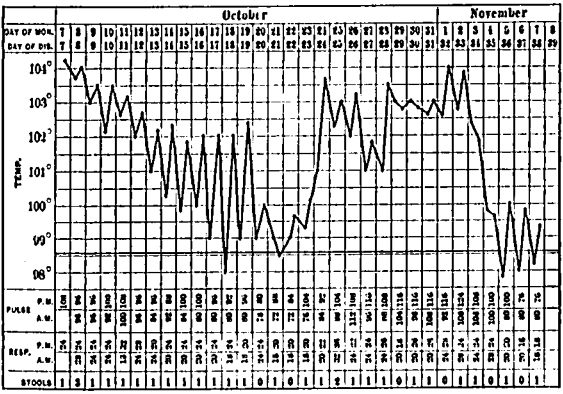
[3] A New Pathogenic Bacillus Isolated from a Case Diagnosed as Typhoid Fever. Thompson Yates Laboratories, 1902, vol. iv. p. 385.

Strong[1] has quite recently reported an autopsy forty-two hours after death in which a bacillus similar to Cushing's Bacillus "O" was isolated from the spleen. The spleen was enlarged and soft, and the organs in general showed the lesions common in acute infections. Both large and small intestines were normal throughout. No agglutination tests were made, and Strong himself suggests the possibility that the bacillus might be a post-mortem invader.

Coleman and Buxton's case 7 has recently been reported in this journal.[2]

The following case occurred in the service of Dr. S. W. Lambert at the New York Hospital. Its similarity to many of the above cases justifies it being placed in the same class with them, and it is reported here as adding another to this interesting group.

J. N., stoker, aged thirty-four years, single. Entered the New York Hospital October 7, 1901. Family and past history unimportant. He never had had typhoid fever. He became ill about seven days before admission, after a heavy debauch. Since then he has had constant vomiting, severe headache, and moderate cough, with white mucus expectoration. He has been continually feverish, and at times chilly, but has had no shaking chills. A mild diarrhœa with two or three passages a day had persisted from the onset up to the time of admission. He was admitted with a temperature of 104.2° F., respirations 24, and pulse 108 per minute. On examination the tongue appeared heavily coated in the centre, with clean red edges and tip. Over both



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[1] Paracolon Bacillus. Johns Hopkins Hospital Bulletin, 1902, vol. xiii. p. 107.

[2] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, June, 1902.

lungs a few sibilant and sonorous râles were heard. The abdomen was distended and tympanitic and showed a few rose-colored spots, which disappeared on pressure. The spleen was not made out. The urine contained a very faint trace of albumin, with occasionally a few hyaline and finely granular casts.

After admission the bowels were constipated, frequent enemata being necessary. The feces presented nothing characteristic, usually being formed and yellowish without the presence of blood or of mucus. The pulse-rate was not increased in proportion to the fever during the earlier period of the disease. The temperature showed a continuous course up to about the thirteenth day, ranging mostly from 102° F. to 104.4° F. After this it became remittent, and on the twentieth, twenty-first, and twenty-second days was normal. It then rose once more, and the second course of fever lasted to the thirty-fifth day. On the twenty-fifth day pain was complained of in the left axilla and over this area loud friction sounds were heard. On the twenty-eighth day the patient had a chill lasting a half-hour. On the next day signs of a small area of consolidation were discovered near the spine of the left scapula. These signs lasted only two days. Leucocytes on the twenty-fifth day, 12,000. No fresh rose-spots appeared during the second course of fever. The abdomen remained rather distended. The spleen was not felt at any time.

The blood serum agglutinated typhoid bacilli fairly well, but not typically, in a dilution of 1 to 10 on the ninth, the nineteenth, and thirtieth days. No agglutination occurred in a dilution of 1 to 50, and no intermediate dilutions were used. Blood cultures were taken on the eleventh day of the first fever, and on the fourth and tenth days of the second course of the fever. The first and last cultures were negative in result. On the second occasion one flask showed a growth of a bacillus which we shall call for convenience Bacillus "Noonan." It was found that the patient's serum agglutinated this organism in a dilution of 1 to 100.

This case, therefore, presented all of the essential clinical features of enteric fever except the presence of a palpable spleen and a Widal reaction toward typhoid bacilli. It is possible that the spleen was enlarged, but was not palpable on account of the distention. The second fever was regarded as a relapse, with a complicating small area of bronchopneumonia. The reasons for not regarding this rise of temperature as due to the bronchopneumonia alone were the limited extent of the signs and their duration of only two days, the lack of an increase in the rate of respirations, and the presence of the B. "Noonan" in the blood at this time.

The B. "Noonan" was found to be a short bacillus decolorizing by the Gram method. In early bouillon cultures the majority of the organisms are motile, the motion being more darting in character than that of typhoid bacilli. The growth in agar, in gelatin, and in bouillon could not readily be distinguished from that of the typhoid bacillus. Milk is at first acidified, but after a period of about three weeks it becomes neutral, and remains so or becomes faintly alkaline.

The amount of alkali developed in plain milk after two months' growth was not sufficient to cause opalization. Indol was not formed after five days' growth in Durham's solution. The bacillus ferments glucose with the production of acid and the evolution of gas, but has no effect upon lactose or sucrose. On the Hiss semisolid "tube" medium there is abundant production of gas, with growth along the stab and out from it in radiating comma-shaped streaks, a typical "colon-growth." The organism differs, therefore, from the typhoid bacillus in that it produces gas in glucose, and does not cause a diffuse clouding of the Hiss semisolid medium. It differs from the colon bacillus in not fermenting lactose, not coagulating milk, and not, at least readily, producing indol.

The agglutination reaction affords a most delicate method for differentiating organisms. Durham has shown, however, that agglutination reactions are by no means absolutely reliable tests of the affinity of bacteria. On the one hand, organisms easily distinguishable, either by their morphology or by their cultural characters, may interagglutinate; that is, the serum derived from an animal immunized with the one will agglutinate the other. On the other hand, organisms which cannot be distinguished with certainty by means of their cultural or morphological characters may show absolutely no tendency to interagglutinate. This is especially true in the colon group, where it is uncommon to find two varieties of colon bacilli giving the same serum reaction. Typhoid bacilli show only minor differences in this respect toward potent typhoid sera.

Gwyn's paracolon bacillus and Cushing's Bacillus "O" illustrate that closely related organisms may show no mutual serum reaction. Thus, Cushing showed that after inoculating a rabbit with his Bacillus "O" and then with B. chol. suis, its serum, while agglutinating these two organisms in a dilution of 1 to 5000, did not affect the paracolon bacillus in a dilution of 1 to 10. On the other hand, Durham states that a Gwyn serum active up to 1 to 20,000 on Gwyn had not the slightest effect upon Cushing's bacillus "O" at 1 to 100 dilution. Schottmüller found that the blood from his patients in each case agglutinated the organism from the same patient in dilutions of from 1 to 100 up to 1 to 10,000. When the serum from one patient was tested with the organism from another, however, the results varied. In the majority of the cases agglutination occurred in dilutions up to 1 to 10,000, but in a few there was no reaction in a dilution of 1 to 33. None of his sera agglutinated typhoid bacilli in the dilution of 1 to 33.

The reaction of B. typhosus, the paracolon bacillus, Bacillus "O" and B. "Noonan" toward Noonan's and toward typhoid sera showed the results tabulated below. As a rule, only two dilutions were made—1 to 10 and 1 to 50.

	Serum of Noonan.	Typhoid sera.					
		1	2	3	4	5	6
B. typhosus . . .	? 1-10 — 1-50	+ 1-100	+ 1-50	+ 1-50	+ 1-50	+ 1-50	+ 1-50
Gwyn	+ 1-100	? 1-10	— 1-10	— 1-10	— 1-10	? 1-10	— 1-10
Cushing	+ 1-50 ? 1-100	? 1-10	— 1-10	— 1-10	— 1-10	? 1-10	— 1-10
B. "Noonan" . .	+ 1-100	— 1-10	— 1-10	? 1-10	— 1-10	? 1-10	— 1-10

? = a suggestive but not typical reaction.

These results may be summed up in the statement that while Noonan's serum agglutinated typhoid bacilli only fairly well in a dilution of 1 to 10 and not at all in a dilution of 1 to 50, it agglutinated B. "Noonan," Gwyn's paracolon, and Cushing's Bacillus "O" in dilutions of from 1 to 50 to 1 to 100. On the other hand, typhoid sera having a potency of at least 1 to 50 gave only suggestive or no reactions with these organisms in dilutions of 1 to 10. In addition to those tabulated, numerous other agglutination tests were made with typhoid sera on B. "Noonan," but in no case was a positive result obtained.

A guinea-pig was immunized by means of intraperitoneal injections of B. "Noonan" and its serum was used for agglutination tests. In addition to Gwyn's and Cushing's organisms several others, belonging apparently to the same group, were tested.

Organisms.	*Dilution of serum.*	*Result.*
B. "Noonan"	1-5000	Positive.
Gwyn's paracolon	1-5000	"
Johnston's Badach	1-5000	"
Schottmüller's Müller (type "A") . .	1-5000	"
Cushing's Bacillus "O"	1-5000 1-500	Suggestive. Positive.
Johnston's Milefsky	1-5000 1-500	Negative. Positive.
Coleman and Buxton's Case 7 . . .	1-500 1-100	Suggestive. Positive.
Kurth's bacillus	1-20	Negative.
Schottmüller's Seeman (type "B") . .	1-20	"
Strong's bacillus	1-20	"
B. typhosus (1 variety)	1-20	"
B. coli (2 varieties)	1-20	"

The above serum reactions suggest the close relationship of the first seven of these organisms. To these and to the infections which they caused are especially applicable the names of paratyphoid bacilli and paratyphoid fever. Whether the remaining organisms are only variations from this type or are to be placed in a separate class or classes can only be determined by careful comparative studies of their cultural and agglutinative peculiarities.